PESTICIDES BRANCH AND
DIVISION OF PHARMACOLOGY

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Division of Food

American Cyanamid Company
New York New York
(AF 14-731)

Evaluation of residue data and method of analysis for HCN residues in grain (P.P. #195).

The American Cyanamid Company seeks to increase an existing tolerance of 25 ppm for hydrogen cyanide residues to 75 ppm on the following grains:

barley, buckwheat, corn (including popcorn), milo (grain sorghum), oats, rice (rough and polished), rye, and wheat.

P.P. #38 resulted in the establishment of the 25 ppm tolerance on all these grains except buckwheat, oats, and sorghum. This tolerance was extended to cover the latter three grains as a result of P.P. #94.

Fumigation is accomplished with liquid HCN (96-98%) or discoids (96% HCN-4% inert) at the rate of 2-4 lbs liquid HCN per 1000 ft^3 of storage with the higher dosages required for milo. The fumigation manual which is included in Section B of the petition states that ".....the period of aeration under the most favorable conditions (ample air circulation and temperature not under 70°F) should not be less than 72 hours." The warehouses will usually be fumigated once a year, in accordance with normal practice.

The dosages listed in the manual included with P.P. #38 were 8 ozs/1000 ft^3 (flour and cereal meals) and 16-24 ozs/1000 ft^3 (rice mills); however our considerations at that time included dosages of 4 lbs/1000 ft^3 which would be used in vacuum chambers.

The method used is a modification of the A.O.A.C. method for HCN in beans. It has been validated for wheat and is considered satisfactory for use on grains. No interferences would be expected from the fumigants exempt from the requirements for a tolerance or from the pesticides with established tolerances on the grains involved. The distillation procedure would be expected to provide for complete distillation of the HCN residues in grain.

The residue data show that the average residues will probably not exceed the 75 ppm tolerance requested but they also show that the maximum residues for wheat, milo maize and possibly those for rice will fall between 75 and 100 ppm.

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Baking studies show that bread made from flour milled from wheat containing as much as 135 ppm HCN contains no HCN residue. Since all grains are processed and heated (cooked or baked) before they are consumed by humans there will be little or no residue of HCN in the food processed from grains bearing the tolerance amount of HCN.

Conclusions

The method of analysis is satisfactory, specific for HCN residues on grains and adequate for the enforcement of the proposed tolerance.

The residues from the recommended use may be in excess of 75 ppm but will not exceed 100 ppm HCN.

Little or no residues of HCN will be present in human foods processed from grains containing 100 ppm HCN.

Recommendations

If pharmacological considerations permit, we recommend the establishment of a 100 ppm tolerance for HCN residues on the grains for which a tolerance is requested.

Detailed Considerations

Method of Analysis

The method used is a modification of the A.O.A.C. procedure for HCN in beans (8th Ed., Method 22.56). It is based on the steam distillation of HCN from an acid solution, the absorption of the evolved HCN in an alkaline solution and titration with silver nitrate.

The blank values on untreated grains are rather high and variable--3.3 to 17.3 ppm for wheat, 3.2 to 13.0 ppm for milo maize, 3.2 to 5.4 ppm for corn and 2.2 to 7.6 for rice--but are considered acceptable in view of the 75 ppm tolerance being requested.

As originally submitted for filing, data were presented showing recoveries of 95% 24 hours after the addition of 100 ppm HCN to wheat but only 54 to 58% after 1 month storage in a closed system. The petitioner claimed that the low recovery was probably due to absorption by rubber stoppers in the test apparatus or hydrolysis, but we considered it as a possible indication of an irreversible reaction with wheat. This deficiency, together with an inadequacy in the pharmacological data, formed the basis for our refusing to file the petition. Additional recovery data were then obtained showing 104 per cent recovery 24 hours after the addition of 100 ppm HCN to wheat and, after 30 days storage in a closed system (in which glass had been substituted for the rubber fittings used in the previous study), recoveries of 70 and 76 per cent in the absence and in the presence of wheat. A reasonable claim is made that the losses which did occur resulted from diffusion of HCN through the four greased glass fittings in each storage flask. However, the essentially similar recoveries in the presence and in the absence of wheat show that no irreversible reaction occurs with wheat during the test period and that the distillation procedure is acceptable from the viewpoint of completeness of HCN extraction.

None of the fumigants now exempt from the requirement for a tolerance or any of the pesticides having established tolerances on these grains would be expected to interfere with the HCN residue analysis.

On the basis of past acceptance of the basic method and a satisfactory recovery with wheat, we now consider the method acceptable for determining HCN residues in grain.

Residue Data

Residue studies are presented for four of the grains involved in this study--wheat, corn, rice and milo maize. These studies consist of residue determinations, usually over a 30 day period, after commercial fumigations of bulk grain stored in the various structures now being used for such storage. The dosages used are those recommended for use, 2 to 4 lbs/1000 ft^3. Grain samples were taken for residue determinations at given time intervals at various depths from the surface to the bottom. In most cases the grain, after the fumigation period, was allowed to aerate naturally without forced aeration.

The HCN residues at the various levels of the grain vary appreciably. This variation is understandable if we consider the very large quantities of grain being fumigated, 20,000 to 250,000 bushels, and the consequent lengthy time interval necessary for equilibrium to be reached. For the purposes of our evaluation, we have averaged all of the residues at the levels used for each study at each time interval and considered the average residue reasonably representative of the HCN residue of the grain at the given time interval.

Wheat - Nine studies are reported, seven at 2 to 2-1/2 lbs/1000 ft^3, one at 3-1/2 and one at 4 lbs/1000 ft^3. Since the residues reported are not directly proportional to dosage, we have averaged them for each time period used in the studies.

The residues are tabulated below:

Time period (days)	Average Residue (ppm)	Residue Range (ppm)
0	34.6	18.8 - 54.7
7	35.8	17.8 - 58.4
14	31.8 (4 lb dosage only)	19.5- 68.1
21	56.2 (4 lb dosage only)	51.9 - 60.5
30	17.6	11.9 - 33.9

Since the large bulk of the residue data were obtained at the 7 and 30 day intervals, we are placing major reliance on the residues at these intervals. They show the need for a tolerance higher than the present tolerance of 25 ppm and show also (if we except the single 4 lb study) a decrease in magnitude of the residues with time, although the decrease is not as rapid as might be expected.

When we plot all values and project an estimated maximum residue at 3 days (a minimum aeration period of 72 hours under the most favorable conditions--ample air circulation and 70°F--is recommended) we arrive at a value of 95 ppm.

Also included for consideration is a USDA study on an experimental fumigation of 41,000 bushels of wheat at the high rate of 4.8 lbs/1000 ft^3. The results show that equilibrium conditions are approached after two to three weeks. They also show that the aeration possible in the closed Quonset structure used for this test over a 6 month period did not reduce the level of residue from that prevalent during the first month of storage, 18 to 44 ppm--depending on the level sampled.

When the wheat from the USDA test was moved into trade channels after the 6 month test period, it was subjected to forced aeration for 75 hours, augered, transferred to an elevator and finally into a box car for shipment. In spite of all the aeration incident to the above movement and handling, only augering caused any reduction in residue level (about 25 per cent), the final residue moving interstate being 19.5 ppm. While the results of this study are surprising as to the constancy of residues in storage and after movement, they should not be accepted as typical, at least as regards loss of HCN residues from movement, since the ambient temperature at the time the grain was moved into trade channels was 18 to 24°F.

Conclusion - Since the bulk of the residues obtained from the 2 to 2-1/2 lb dosages reflect the need for a tolerance in excess of 75 ppm and since the maximum 4 lbs/1000 ft^3 dosage may result in residues in the neighborhood of our projected maximum, we conclude that a tolerance of 100 ppm rather than 75 ppm is necessary to cover residues from this usage of HCN in wheat.

Corn - Three studies were conducted, two at the minimum rate (2 lbs/1000 ft^3) and one at close to the maximum rate (3.8 lbs/1000 ft^3). Only 0 and 7 day studies were conducted. Here, as in the case of wheat, residues are not proportional to dosage. The residues were therefore averaged for the time intervals used, the 0 day residue averaging 34.3 ppm (range 11.9 to 51.9 ppm) and the 7 day residue averaging 12.7 ppm (range 8.6 to 16.5 ppm).

When we plot these values and project maximum values, we arrive at 52 ppm at 0 days and 35 ppm at the recommended 3 day aeration period.

HCN apparently dissipates more rapidly from corn than from wheat, possibly because of the lower bulk density of the former.

In one of the studies, corn with a surface residue of 8.6 ppm 7 days after fumigation was "turned" and the surface residue was then found to be higher, 19.5 ppm. "Turning" would normally result in lower residues since the grain is aerated in the process. Since mixing also occurs in the "turning" process, we feel that the higher value after "turning" is more representative of the actual residue in the grain than the value determined before "turning."

Conclusion - We conclude that a tolerance of 75 ppm would be adequate for residues of HCN on corn from the recommended usage.

Milo Maize - Five studies are reported and consist of residues determined over a 30 day period--46 days in one study--from a dosage of 3 lbs/1000 ft^3. The residues are tabulated below:

Time period (days)	Average residue (ppm)	Residue range (ppm)
0	60.7	23.8 - 81.2
7	50.8	33.2 - 71.2
30	42.9	27.6 - 51.7
46	34.1	32.4 - 35.7

These residues also show a decrease with time but not as rapid a decrease as might be expected.

A plot of the values shows projected maximum residues of 81 ppm at 0 days, 78 ppm at 3 days.

Conclusion - Since the higher dosages are used for milo and since 4 lbs/1000 ft^3 dosages may result in even higher residues than those reported, we conclude that a tolerance of 100 ppm rather than 75 ppm is necessary to cover residues on milo from this usage.

Rice - Two sets of studies were made, one on rough and one on milled rice.

Rough rice - Two studies at the rate of 2.5 lbs/1000 ft^3 show the following results:

Time period (days)	Average residue (ppm)	Residue Range (ppm)
7	37.0	27.6 - 46.3
19	37.0*	--
30	31.6*	--
34	36.0*	--

*One study only.

Milled rice - Three studies were made with the sole purpose of determining possible "build-up" of residues from repeated fumigations (10 to 11 in number) at the rate of 1 to 2.5 lbs/1000 ft^3 over a period of 12 to 16 months. The residues obtained in the 3 studies were 65.3 ppm about a month after the last fumigation (20.1 ppm after 7 days aeration in a cloth bag), 88.6 ppm about 4 months after the last fumigation but with no aeration through the fumigation period (15.8 ppm after 7 days aeration in a cloth bag), and 38.8 ppm within a month after the last fumigation (23.8 ppm after 7 days aeration in a cloth bag). These results show that no "build-up" of residues occurs from repeated fumigations of milled rice. The hull and bran have been removed in the milling and in the case of wheat the HCN residues concentrate in the bran (as will be noted later); we therefore cannot translate the lack of residue build-up in milled rice directly and completely to unprocessed grains. It should be noted that "build-up" of residues is not to be anticipated since the grain would normally be fumigated only once a year.

Conclusion - If we consider residues which may result from the maximum dosage and those from repeated fumigations, a 100 ppm rather than a 75 ppm tolerance on rice is necessary.

Discussion

The evaluation of the residue data given in this petition makes the necessity for an increase in the present tolerance of 25 ppm apparent. Data presented in support of the original request for a tolerance on grains, P.P. #38, indicated that a 25 ppm level would be adequate from a maximum dosage of 4 lbs/1000 ft^3. As data accumulated after the establishment of the 25 ppm tolerance, the need for an increased tolerance became evident. The petitioner is requesting a 75 ppm tolerance and the average residues from the usage will probably not exceed this level. However, the maximum residues in all probability will exceed this level and we are therefore recommending the establishment of a 100 ppm tolerance. We recognize the possible impact of a four fold increase in an established tolerance but, if the present usage of HCN for grain fumigation is to continue, the tolerance established should reflect the magnitude of the residues likely to result.

In considering the 100 ppm tolerance we are recommending, it must be borne in mind that whatever the level of residue in the grain, the final items of human consumption will contain little or no HCN residues since all of the grains are washed, processed and/or heated before reaching our diet. As an example, data are presented showing that white and whole wheat bread baked from flour milled from wheat containing as much as 135 ppm HCN contain no HCN residues. From the data, we estimate that white and whole wheat flour milled from wheat bearing 100 ppm HCN would contain < 20 ppm and < 30 ppm HCN, respectively. The residues concentrate in the bran and the shorts (the germ contains 1/4 to 1/3 of the residue in the bran) but these items in their various food usages are also subjected to washing, processing and/or heating before they become items of our diet. Since details of this study may be of interest, they are tabulated below. It should be noted that the intermediate products probably received only a very short aeration.

HCN Residues in Wheat, Flour & Bread (ppm)

Material	Sample				
	A*	C	D	E	F
Wheat (as rec'd)	2.2	66.6	15.1	59.4	135.0
bran	4.3	109.4	23.8	71.3	112.4
shorts	4.3	103.5	10.8-13.0	51.8-58.3	86.4-101.6
germ	4.3	--	6.4	26.0	43.2
flour (white)	2.2	15.1	4.4	4.4-6.4	15.2-17.2
flour (whole wheat)	4.3	--	6.4	15.2	38.8
bread (wheat)**	1.1	trace	1.1	1.1	1.1
bread (whole wheat)**	1.1-2.1	--	1.1	1.1	2.1

*Control - no HCN treatment.
**No HCN residues are present in bread, all values being equivalent to or less than the blank values.

Bran is an item of cattle feed and, since bran destined for such a purpose is not further processed, some concern might be felt for the effects of any HCN residues remaining at the time of consumption, particularly as regards possible meat and milk contamination. No actual meat and milk residue studies are presented, but the Division of Pharmacology assures us that HCN at the tolerance level is so readily and rapidly metabolized in the animal that no meat and milk residues will result.

No residue data are presented for barley, buckwheat, oats and rye but we consider the residue data presented sufficient to cover these grains.

Conclusion

A 75 ppm tolerance may suffice for some of the grains involved in this petition but the necessity for a 100 ppm tolerance for wheat, rice, and milo maize leads us to the conclusion that a 100 ppm tolerance for all of the grains is indicated.

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